REMARKS

Claims 1, 3-15 and 17-21 are pending in the present application. Claims 11-15 and 19 have been withdrawn. Claim 1 is in independent form. Claim 1 is amended. In view of the above amendments and following remarks, favorable reconsideration and allowance of the present application is respectfully requested.

I. STATEMENT REGARDING SUBSTANCE OF TELEPHONE INTERVIEW

In response to the Interview Summary mailed on May 21, 2009 and the telephonic interview conducted on May 19, 2009 between Examiner David C. Thomas and Applicants' representatives, Crystal Wilson (Reg. No. 61,730), the following remarks are respectfully submitted in connection with the above-identified patent application.

Initially, Applicants wish to thank the Examiner for agreeing to, and conducting, the interview. In the telephonic interview, Applicants' representatives discussed the differences between the methods and materials used in the separation methods taught by Cheng and Frechet, and various reasons why the differences teach away from the combination of the references.

Applicants' representatives also discussed the method taught by Hodko wherein redox markers (*i.e.*, labels) capable of intercalating into ds-DNA molecules are used for detection, and the differences between the electrode arrangement in Cheng and Hodko. Applicants' representative also

discussed the lack of motivation to combine the teachings of Hodko and Cheng.

Furthermore, both parties acknowledged that amending the claims to emphasis the exclusion of labels may help further distinguish over the cited art, specifically the markers taught by Hodko.

II. CLAIM AMENDMENTS

By the present Amendment, Applicants submit that claim 1 has been amended. The amendment to claim 1 is supported, at least, by paragraph [0018] of the originally-filed Specification. Thus, Applicants submit that the amendment does not introduce new matter.

III. CITED ART GROUNDS OF REJECTION

(A) Claims 1, 3, 4, 7, 8, 17, 20 and 21 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng et al. (hereinafter "Cheng"), U.S. Patent Publication No. 2002/0155586 A1 in view of Frechet et al. (hereinafter "Frechet"), U.S. Publication No. 2004/0101442 A1 and further in view of Hodko et al. (hereinafter "Hodko"), Detection of Pathogens Using On-Chip Electrochemical Analysis of PC Amplified DNA Molecules, Proceedings of SPIE, Vol. 4265, p. 65-74 (2001). Applicants respectfully traverse the rejection.

i. INDEPENDENT CLAIM 1

Independent claim 1 is directed to a method for PCR amplification and detection of nucleotide sequences including (*inter alia*) "detecting hybridization events on the probe molecules immobilized at one of the analytical positions electrochemically with the aid of a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement and a label is excluded from the detected nucleotide sequences." Applicants submit that the combination of Cheng, Frechet and Hodko fails to explicitly teach, or otherwise suggest, the above features recited in amended independent claim 1.

a. CHENG, FRECHET AND HODKO

Acknowledging the deficiencies of Cheng, the rejection states that "Cheng also does not teach a method wherein detected nucleotide sequences alter impedance of the microelectrode arrangement." Action, p. 6. However, "Hodko teaches a method for detection of pathogens based on electrochemical detection of PCR amplified molecules specific for the pathogen wherein the detection method is based on electrochemical AC impedance analysis using redox probes capable of intercalating into double-stranded DNA products in contact with platinum electrodes (p. 66, lines 16-19 and p. 68, lines 1-12)." Action, p. 6.

Hodko, directed to a microfluidics based system that utilizes electrochemical detection of the PCR amplified DNA molecules specific for a targeted pathogen, teaches that "[a]n impedance spectroscopy based method

is used to detect DNA amplicons in the presence of DNA intercalating redox probe, which further amplifies the detection signal." Hodko, *Abstract.* Hodko further teaches that "[i]n the presence of redox mediators capable of intercalating into the DNA molecule, this signal is electrochemically amplified. A number of redox-probes were tested to determine which of the probes provide the largest signal in the presence of DNA." Hodko, p.68. Thus, Hodko teaches ds-DNA molecules are detected using impedance measurements after intercalation with redox markers. In other words, the redox markers are bound to the ds-DNA, then the signal of the markers is detected. Thus, the redox markers (*i.e.*, labels) are required, and not "excluded from the detected nucleotide sequences" as recited in amended independent claim 1.

Regarding the alleged combination of Cheng and Hodko, the Examiner states that "...the use of redox probes as taught by Hodko is for purposes of detection only...[t]he probes simply intercalate into the bound DNA to provide a means of detection based on the AC impedance detection step, and thus the impedance of the electrode-based system of Cheng would be altered during a detection step to indicate a signal." Advisory Action mailed June 2, 2009, p. 2. Thus, in the combination alleged by the Examiner, the redox markers of Hodko are used in the electrode-based system of Cheng.

For at least these reasons, Applicants submit that Cheng in view of Frechet and further in view of Hodko fails to explicitly teach, or otherwise suggest, a method for PCR amplification and detection of nucleotide sequences including "detecting hybridization events on the probe molecules

immobilized at one of the analytical positions electrochemically with the aid of a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement and a label is excluded from the detected nucleotide sequences" as recited in amended independent claim 1.

Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to independent claim 1, and claims 3, 4, 7, 8, 17, 20 and 21 at least by virtue of their dependency on independent claim 1.

B) Claims 5 and 6 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Frechet and Hodko and further in view of Ghodsian, U.S. Publication No. 2002/0115293 A1. Applicants respectfully traverse the rejection.

Ghodsian is directed to a chip device for sequencing long DNA fragments using optical detection. Ghodsian fails to teach, or suggest, electrochemical detection using a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement and a label is excluded from the detected nucleotide sequences. Thus, Ghodsian fails to cure the deficiencies of Cheng, Frechet and Hodko with respect to independent claim 1.

Applicants submit that claims 5 and 6, at least by virtue of their dependency on independent claim 1, are patentable over the combination of Cheng, Frechet, Hodko and Ghodsian.

As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to claims 5 and 6.

(C) Claims 9, 10 and 18 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Cheng in view of Frechet and Hodko and further in view of Strizhkov et al. (hereinafter "Strizhkov"), PCR Amplification on a Microarray of Gel-Immobilized Oligonucleotides: Detection of Bacterial Toxin- and Drug-Resistant Genes and Their Mutations, BioTechniques, 29(4):844-846, 848, 850-852, 854, 856-857 (Oct. 2000). Applicants respectfully traverse the rejection.

Strizhkov, directed to PCR amplification, teaches that "[t]he kinetics of amplification was measured in real time in parallel for all gel pads with a fluorescent microscope equipped with a charge-coupled device (CCD) camera." Strizhkov, Abstract. Thus, Strizhkov teaches using optical detection, not electrochemical detection using a microelectrode arrangement wherein detected nucleotide sequences alter impedance of the microelectrode arrangement and a label is excluded from the detected nucleotide sequences. Thus, Strizhkov fails to cure the above-noted deficiencies of Cheng, Frechet and Hodko with respect to amended independent claim 1.

Applicants submit that claims 9, 10 and 18, at least by virtue of their dependency on independent claim 1, are patentable over the combination of Cheng, Frechet, Hodko and Strizhkov.

As such, Applicants respectfully request that the Examiner reconsider and withdraw the rejection to claims 9, 10 and 18.

IV. REQUEST FOR REJOINDER

In the event that independent claim 1 is held allowable, Applicants respectfully request rejoinder of withdrawn claims 11-15 and 19, which depend from and therefore require all of the features of claim 1.

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CONCLUSION

Accordingly, in view of the above, reconsideration of the rejections and allowance of each of claims 1, 3-15 and 17-21 in connection with the present application is earnestly solicited.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 08-0750 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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